REMARKS

This document is filed in reply to the Office Action dated August 23, 2005 ("Office Action"). Applicant has amended claim 12 to specify a feature of the claimed subject matter. Support for the amendment can be found in original claim 1. No new matter is introduced.

Note that, in response to the restriction requirement dated July 15, 2005, Applicant elected for prosecution Group I, i.e., the claims "drawn to an isolated nucleic acid sequence comprising a nucleotide sequence at least 70%, 80%, 90%, 95%, 100% identical to SEQ ID NO:1, a cell comprising said nucleotide sequence, an isolated nucleic acid that hybridizes under stringent conditions to SEQ ID NO:1, or a complementary sequence thereof, and a method of expressing said isolated nucleic acid that hybridizes to SEQ ID NO:1, in a cell (emphasis added)." Among all pending claims, claim 12 covers "an isolated nucleic acid that hybridizes under stringent conditions to SEQ ID NO:1" and therefore is a member of Group I. However, in the Office Action, the Examiner apparently withdrew, through an oversight, claim 12. See the Office Action, page 2, lines 4-5. Applicant respectfully requests that claim 12 be considered in this application.

Claims 1-28 are pending. Among them, claims 7-11, 13, and 15-28 have been withdrawn from further consideration for covering a non-elected invention. Thus, only claims 1-6, 12, and 14 are under examination. Reconsideration of the application is respectfully requested in view of the remarks below.

Double patenting

The Examiner provisionally rejected claims 1-6 and 14 under 35 U.S.C. § 101 for statuary type double patenting. According to the Examiner, the claims "claim[] the same invention as claims 1-6 and 14 of copending Application No. 10/881,758 ("the '758 application")." See the Office Action, page 3, lines 19-21.

Applicant disagrees. As the Examiner correctly acknowledged, "the term 'same invention,' in this context, means an invention drawn to identical subject matter." See the Office Action, page 2, lines 11-12 and MPEP 804II. In this application, claims 1-6 and 14 respectively

cover (a) isolated nucleic acids, each of which contains a nucleotide sequence at least 70% identical to the sequence of NV-F (SEQ ID NO:1), or a complementary sequence thereof; and (b) cells containing and expressing such nucleic acids. In contrast, claims 1-6 and 14 in the '758 application respectively cover (i) isolated nucleic acids, each of which contains a nucleotide sequence at least 70% identical to the sequence of Colon-V, or a complementary sequence thereof; and (ii) cells containing and expressing such nucleic acids.

Applicant would like to point out that the sequences of NV-F and Colon-V are different. Indeed, they are 364 and 509 nucleotides in length and encode two different proteins of 121 and 116 amino acids in length, respectively. To the extent that the sequences of NV-F and Colon-V are different, the rejected claims do not claim "the same invention as that of claims 1-6, and 14 of copending Application No. 10/881,758." Thus, it is respectfully requested that the rejection be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph (enablement)

The Examiner rejected claims 1-6 and 14 for lack of enablement on a number of grounds. See the Office Action, page 3, second paragraph. As mentioned above, claims 1-6 and 14 respectively cover (a) isolated nucleic acids, each of which contains a nucleotide sequence at least 70% identical to SEQ ID NO:1, or a complementary sequence thereof; and (b) cells containing and expressing such nucleic acids. The presence of the nucleic acid in a subject predisposes the subject to an abnormal liver condition, an adenocarcinoma, or a combination thereof. Applicant respectfully traverses each of the Examiner's grounds below.

I

It is the Examiner's position that "the specification has failed to disclose any cell comprising SEQ ID NO: 1 or a protein produced by SEQ ID NO: 1. There is no disclosure of any *in vitro* data that would lead to the skilled artisan to believe that SEQ ID NO: 1 codes for any protein. ... The specification provides no guidance as to what cell, if any harbors SEQ ID NO: 1. The specification fails to disclose the claimed cell of the invention comprising SEQ ID NO: 1 in an *in vivo* or *in vitro* embodiment." See the Office Action, page 6, lines 1-4 and lines 16-18.

Applicant notes that, according to MPEP 2164.02, "[c]ompliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed" and "[t]he specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation." The present specification provides general teachings as to how to express nucleic acids of claims 1-6 in host cells to make proteins encoded by the nucleic acids. See, e.g., pages 5-6, carryover paragraph. As all techniques required are routine, "one skilled in the art will be able to practice it without an undue amount of experimentation." In fact, as shown in the Declaration by Dr. Chau-Ting Yeh (attached hereto as "Exhibit A"), a nucleic acid covered by claims 1-6 indeed codes for a protein. The declaration also demonstrates that transfected insect host cells and a patient's hepatocytes contain and express SEQ ID NO: 1. In view of the above remarks, Applicant submits that the Examiner's position is untenable.

II

The Examiner also asserted that "the specification fails to disclose [examples] of an abnormal liver condition in subjects expressing an isolated nucleic acid sequence at least 70%, 80%, 90%, or 95% identical to SEQ ID NO: 1. The specification has taught only the identification of ... SEQ ID NO: 1 in subjects suffering from non-A-E hepatitis, chronic hepatitis B, chronic hepatitis C, and colon cancer." See the Office Action, page 6, lines 4-9.

Applicant disagrees. As pointed out in MPEP 2164.03 and quoted above, "[t]he specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation." Here, the specification teaches that the expression of SEQ ID NO: 1 and the protein encoded by it (SEQ ID NO: 2) indicates that a subject is predisposed to an abnormal liver condition (such as non-A-E hepatitis, chronic hepatitis B, or chronic hepatitis C) or colon cancer. See, e.g. page 6, lines 17-22. Dr. Yeh's declaration also demonstrates that the protein (SEQ ID NO: 2) correlates with an abnormal liver condition. Since the protein can be encoded by SEQ ID NO: 1 or its degenerate variants, one skilled in the art would recognize that subjects expressing the degenerate variants will also be predisposed to an abnormal liver condition. Given these teachings and the fact that a large number of the degenerate variants are at least 70%, 80%, 90%,

or 95% identical to SEQ ID NO: 1, "one skilled in the art will be able to [make and use these degenerate variants for] practic[ing the claimed invention] without an undue amount of experimentation." Thus, "the specification need not contain an example" as requested by the Examiner.

III

The Examiner further asserted that "it is not known in the art or disclosed in the specification whether SEQ ID NO: 1 results in an abnormal liver condition. The specification only discloses that there is a correlation with the expression of SEQ ID NO: 1 in subjects suffering from an abnormal liver condition (emphasis added)." See the Office Action, page 6, lines 12-15. Applicant would like to point out that the claims at issue entail that the presence of the nucleic acid in a subject predisposes the subject to an abnormal liver condition" but does not result in the abnormal liver condition. Thus, there is no need for the specification to disclose whether SEQ ID NO: 1 results in an abnormal liver condition. More specifically, to show the presence of SEQ ID NO: 1 in a subject predisposes the subject to an abnormal liver condition, the Specification provides a working example proving that SEQ ID NO: 1 was detected by PCR in 6.7% of healthy individuals, 23.5% of patients with chronic non-A-E hepatitis, 54% of patients with chronic hepatitis B, 44% of patients with chronic hepatitis C, and 23.3% of patients with colon cancer, respectively. See the specification, pages 13-14, carryover paragraph.

Accordingly, Applicant submits that claims 1-6 and 14 meet the enablement requirement and requests that the rejection be withdrawn. Claim 12, as amended, is drawn to an isolated nucleic acid that hybridizes under stringent conditions to SEQ ID NO:1, the presence of which in a subject predisposes the subject to an abnormal liver condition, an adenocarcinoma, or combination thereof. For the same reasons set forth above, it also meets the enablement requirement.

Rejection under 35 U.S.C. § 112, first paragraph (written description)

The Examiner rejected claims 1-6 and 14 under 35 U.S.C. § 112, first paragraph for not complying with the written description requirement. See the Office Action, page 7, lines 12-16.

Applicant respectfully traverses and discusses claim 12 first. As mentioned above, claim 12 is drawn to an isolated nucleic acid (i) that contains a strand that hybridizes under stringent conditions to SEQ ID NO:1 or its complement, and (ii) the presence of which in a subject predisposes the subject to an abnormal liver condition, an adenocarcinoma, or combination thereof. Applicant submits that the specification provides sufficient written description for claim 12, as evidenced by the U.S. Patent and Trademark Office's own guidelines on the subject: Synopsis of Application of Written Description Guidelines, www.uspto.gov/web/menu/written.pdf ("Guidelines"). Example 9 of the Guidelines illustrates a hypothetical situation that mirrors the present case. Just as the claim in Example 9, claim 12 is drawn to an "isolated nucleic acid that hybridizes to SEQ ID NO: 1 [or its complement] under highly stringent conditions and encodes a protein with a specific function. Just as in Example 9, "[t]he claim is drawn to a genus of nucleic acids all of which must hybridize with SEQ ID NO: 1 and must [have a] specific activity." Furthermore, "[t]here is a single species disclosed (a molecule consisting of SEQ ID NO: 1) that is within the scope of the claimed genus" and "[t]here is actual reduction to practice of the disclosed species." Example 9 then provides the following guidance to examiners:

> "Now turning to the genus analysis, a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claim because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs. Thus, a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention.
> **Conclusion:** The claimed invention is adequately described."

In view of the very clear instructions from the Guidelines and the teachings in the Specification, Applicant submits that claim 12 meets the written description requirement.

Claims 1-6 cover isolated nucleic acids. Each of the nucleic acids contains a nucleotide sequence at least 70% identical to SEQ ID NO:1, or a complementary sequence thereof; and presence of the nucleic acid in a subject predisposes the subject to an abnormal liver condition, an adenocarcinoma, or combination thereof. It is well known in the art that nucleotide sequence

at least 70% identical to a probe sequence, e.g., SEQ ID NO: 1, would hybridize to the probe or its complement under highly stringent conditions. Thus, for the same reasons set forth above, claims 1-6 also meet the written description requirement.

In addition, Applicant notes that the subject matter of claims 1-6 mirrors that illustrated in Example 14 of the above-mentioned Guidelines. As in the claim in Example 14, claims 1-6, are drawn to a "[nucleic acid] or variants having [at least 70]% identity to SEQ ID NO: [1] and having [a specific] activity are essential to the operation of the claimed invention. The procedures for making variants of SEQ ID NO: [1] are conventional in the art and an assay is described which will identify other [variant] having the ... activity. Moreover, procedures for making [such] variants ... which have [at least 70]% identity to SEQ ID NO: [1] and retain its activity are conventional in the art." Also, as in Example 14,

> [t]here is actual reduction to practice of the single disclosed species. ... The single species disclosed is representative of the genus because all members have at least [70]% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least [70]% identical variants of SEQ ID NO: [1] which are capable of the specified ... activity. One of skill in the art would conclude that applicant was in possession of the necessary common attributes possessed by the members of the genus.
>
> **Conclusion:** The disclosure meets the requirements of 35 USC §112 first paragraph as providing adequate written description for the claimed invention.

Again, in view of the instructions from the Guidelines and the teachings in the Specification, Applicant submits that claim 1-6 meet the written description requirement on this independent ground. Claim 14 covers cells containing and expressing the nucleic acids. For the same reasons, it also meet the written description requirement.

CONCLUSION

Applicant submits that grounds for the rejections asserted by the Examiner have been overcome, and that claims, as pending, define subject matter that meets the written description and enablement requirements and is not claimed in Application No. 10/881,758. On this basis, it is submitted that allowance of this application is proper, and early favorable action is solicited.

Enclosed is a $60 check for the Petition for Extension of Time fee. Please apply any other charges to deposit account 06-1050, referencing the Attorney's Docket No. 14176-003001.

Respectfully submitted,

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